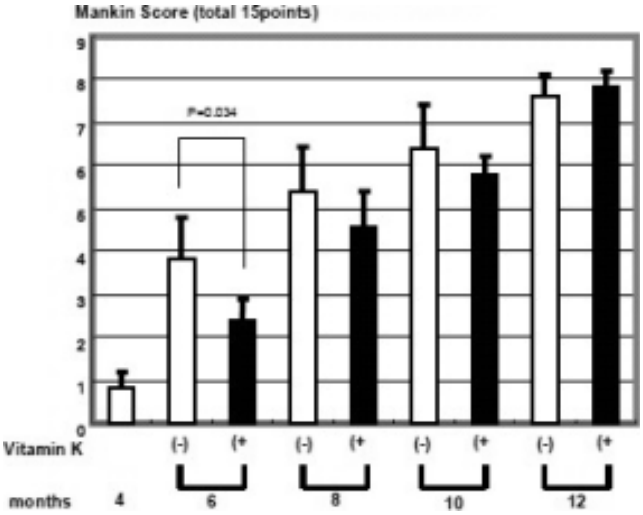

Results: Progressive histopathologic changes characteristic of developing OA were observed concomitantly with aging. This change was initiated by the disruption of the weight-bearing regions of articular cartilage at 6 months of age, and subsequent changes such as cloning of chondrocytes or loss of Safranin-O staining were recognized from 8 months of age onward. The figure shows the Mankin scores obtained from sections stained with Safranin-O. As shown in this figure, the scores were increased with aging in both groups. Statistical significance was recognized between two groups only in the early phase at 6 months ($p = 0.032$). This data was consistent with the data of gross appearance.
Conclusions: The present study demonstrated that menaquinones could delay the progression of osteoarthritis. To our knowledge, this is the first report to discuss the effect of menaquinones on the pathological feature of OA.

531 EFFECT OF HYALURONIC ACID IN SYMPTOMATIC HIP OA: A MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Purpose: To evaluate the efficacy and tolerability of one single hyaluronic acid (Adant®) intra articular (IA) injection for hip osteoarthritis (OA).
Methods: A randomised, double-blind (investigator blinded to the procedure), placebo-controlled trial. Patients (age over 30) with symptomatic hip OA (pain level on VAS >40 mm), Kellgren Lawrence grade II or III, were randomly allocated to receive one fluoroscopically guided IA injection of hyaluronic acid (2.5 ml) or placebo (2.5 ml). Patients were followed up every month for 3 months. The mean outcome measure was the level of pain recorded on a VAS (0–100 mm) at month 3 and compared with baseline. Secondary outcomes included the percentage of responders according to the OMERACT-OARSI criteria, the Western Ontario and McMaster Universities (WOMAC) OA index subscores on pain, stiffness and disability, the patient's and physician's global assessments. Safety was assessed at each visit. Statistical analysis was performed on the inter-group difference in the intent-to-treat population (ITT) and in the per protocol (PP) population. Missing data were replaced by carrying forward the last outcome.
Results: Eighty-five patients were included, and were randomized in the hyaluronic acid group ($n = 42$) or in the placebo group ($n = 43$). Baseline characteristics were similar between the two groups. The number of drops out was 5% ($n = 4$). At end point, the decrease in pain was −7.8 (24.95) and −9.12 (27.37) in the hyaluronic acid and placebo groups respectively, in the ITT population ($p = 0.98$). Same result was found in PP analysis. The OMERACT-OARSI responder rate was 33.3% in the hyaluronic acid group and 32.5% in the placebo group ($p = 0.94$). There was no significant difference, both in ITT and in PP analysis, in secondary end points as well as in the consumption of rescue medication between placebo and verum. There was no difference in the frequency of adverse events between groups.
Conclusions: This study failed to show a superior symptomatic effect of a single IA hyaluronic acid injection (Adant®) over placebo in patients with hip OA. Further studies are required to explore the potential efficacy of more than one single intra articular injection in hip OA.

532 HYALURONIC ACID INTERACTION WITH BUPIVACAINE IN INTRAARTICULAR ADMINISTRATION

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Purpose: Elucidate if a daily common clinical administration of two intraarticular drugs as Hyaluronic Acid (H.A.) used to treat osteoarthrosis and Bupivacaine used as local anaesthesia, cause increase degradation of Hyaluronic Acid.
Methods: *In vitro* studies with five commercial H.A. have been used for this study, (Synvisc®, Coxarthrum®, Go-on®, Hyalgan® and Durolane®) with Bupivacaine at three different concentrations (0.25%, 0.50% and 0.75%) with/without adrenaline (1/200,000), with 24 hours incubation at 4ºC and 37ºC. Cromatography procedures (molecular exclusion HPLC) have been used for determination of molecular weight and degradation percentage of H.A. Anova-Manova and Kendall's correlation have been used to determinate statistscal significance.
Results: Synvisc® and Durolane® have shown less degradation and different behavior than Coxarthrum®, Hyalgan® and Go-on® (Kendall's correlation $p < 0.05$). Temperature of incubation modified the degradation of H.A. Durolane® and Synvisc® at 4ºC showed higher degradation than at 37ºC ($p < 0.05$), otherwise happens for Coxarthrum®, Go-on® and Hyalgan® that increased degradation at 37ºC ($p < 0.05$). Higher concentration of Bupivacaine increased the degradation of H.A. in all cases ($p < 0.05$) and the concomitant use of adrenaline increased the degradation in the three concentrations used at the present study for Synvisc®, 0.25 and 0.75 for Coxarthrum®, only at 0.75 for Durolane® and 0.25 for Go-on® ($p < 0.05$). Adrenaline seems not to increase degradation over Hyalgan.
Conclusions: Bupivacaine administration (with/without adrenaline) with H.A. must be valued before concomitant intraarticular administration because Bupivacaine increased H.A degradation of all the H.A. studied. Durolane® and Synvisc® have shown less degradation (6 to 20%) and different behavior than Coxarthrum®, Hyalgan®, Go-on® (12 to 20%, 27 to 29% and 28 to 39% respectively). Higher concentration of Bupivacaine and the concomitant use of adrenaline increased the degradation of H.A. in all cases except the concomitant use of adrenaline that seems not to affect Durolane® degradation except at highest Bupivacaine concentration.

533 CHRONIC ADMINISTRATION OF CHONDROITIN SULFATE DOES NOT AFFECT CYTOCHROME P450 AND NADPH P450 REDUCTASE IN THE RABBIT

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Purpose: Chondroitin sulfate (CS) is a SYSADOA eliciting an anti-inflammatory effect. Since patients take CS over long periods, it was of interest to assess whether CS modulates the activity of cytochrome P450 isoforms (P450).
Methods: Two models were used, chronic intake of CS in control rabbits and in rabbits with a down-regulated P450 by an inflammatory reaction (IR). Six groups of 5 rabbits were used; three were used to assess the effect of CS on P450, one without CS and two receiving orally around 20 mg/kg/day CS for 20 and 30 days; three groups received turpentine s.c. generating an aseptic IR (AIR) 48 h before their sacrifice, e.g. days −2, 18 and 28, exposed to CS for 0, 20 or 30 days, respectively. CYP3A6, CYP1A2 and NADPH P450 reductase (NADPH) activity, expression and RNAm were assessed in the hepatocytes.
Results: Compared with control rabbits, 20 and 30 days CS did not affect the activity of CYP3A6, e.g. 15582±1330, 13480±3052 and 14701±841, and of CYP1A2, e.g. 6532±1203, 11612±2403 and 7494±746, arbitrary